plicated by other preexisting renal disease. Readministration of the drug will invariably lead to recurrence of the problem and therefore must be avoided.

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Asthmogenic Drugs

CERTAIN DRUGS may adversely affect asthma by exacerbating a previously quiescent asthmatic condition or increasing the severity of established asthma.

The beta-adrenergic blocking drugs propranolol (Inderal) and nadolol (Corgard), when administered in high doses, exacerbate asthma and, therefore, probably should be contraindicated in moderate to severe cases of the disease. In response to beta-blocking therapy, mild coughing and wheezing may reappear in patients whose childhood asthma had been asymptomatic for many years. In mildly asthmatic patients who require these drugs, treatment should be initiated with low doses, such as 5 to 10 mg per day and then slowly increased while monitoring for bronchial obstruction. Metaprolol (Lo-Pressor) more selectively blocks beta-1 (cardiotropic) receptors than beta-2 (bronchodilator) receptors, so the drug has less potential for exacerbating asthma. However, it still must be used with caution in cases of moderate to severe asthma.

Aspirin and other nonsteroidal anti-inflammatory drugs, such as indomethacin (Indocin) and ibuprofen (Motrin), are capable of producing asthmatic attacks in certain patients, presumably by their inhibition of prostaglandin synthesis. Up to 4 percent of asthmatic patients and up to 2 percent of patients with rhinitis will experience asthma following the ingestion of these drugs. The percentage is even higher in patients with nasal polyps and asthma. "Triad asthma" involves a combination of bronchial asthma, nasal polyps and aspirin sensitivity. However, asthma and rhinitis commonly precede aspirin sensitivity, often by many years. Some aspirin-sensitive asthmatic patients react similarly to tartrazine (FD & C No. 5), a yellow coloring agent found in foods and also used in certain medications.

Paradoxical bronchospasm may occur after the inhalation of sympathomimetic aerosols, especially isoproterenol, when the drug has been overused. The mechanism for this phenomenon, however, is unknown. Therapeutic inhalation of sodium cromolyn (Intal) and acetylcysteine (Mucomyst) has been reported to cause bronchospasm by direct bronchial irritation.

Pituitary snuff, pancreatin, and *Bacillus subtilis* enzymes in detergents can cause immunoglobulin E-mediated allergic asthma.

In summary, a detailed drug history is critical to evaluation in newly asthmatic patients and in those with an exacerbation of chronic asthma.

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Why Nocturnal Asthma?

ASTHMA IS WORSE during the sleeping hours and its onset is often heralded by nocturnal coughing or wheezing. Factors attributed to this phenomenon of nocturnal asthma can be classified as mechanical (depressed pulmonary function in the supine position), allergic (bedroom dust, mite and feather allergens), psychological (frightening dreams) and biochemical (decreased serum cortisol levels).

Recent studies have shred fresh light on this subject. An inherent circadian variation in airway resistance is accentuated in patients with asthma. When such patients are subjected to hourly tests of pulmonary function, the best values are found during the afternoon hours and the worst between 10:00 PM and 8:00 AM. The differences are statistically significant and are present even when the patient feels free of symptoms. No correlation has been found between nocturnal asthma and dream states (as measured by rapid eye movement patterns) or nocturnal changes in circulating corticosteroid levels. Furthermore, a steady state infusion of hydrocortisone fails to ablate the circadian rhythm of airway caliber.

Barnes and associates have made some provocative comparisons between biochemical changes and nocturnal asthma. In five subjects with asthma they found decreased plasma epinephrine and cyclic adenosine monophosphate levels at 4:00 AM versus 4:00 PM. Plasma histamine